AMENDED CLAIMS

[received by the International Bureau on 06 August 2004 (06.08.04); original claims 1-15 replaced by amended claims 1-15 (21 pages)]

1. A compound of structural formula (I):

$$A - (CH2)m - (CH2)n - R2$$

$$R1$$
(I)

or a pharmaceutically acceptable salt or a solvate thereof, wherein

R₁ is:

(D)-aryl or (D)-heteroaryl, wherein aryl and heteroaryl are unsubstituted or substituted;

$$(R_5)_s (R_3)_s (R_3$$

A is:

AMENDED SHEET (ARTICLE 19)

each R₃ is independently: hydrogen, halo, alkyl, haloalkyl, hydroxy, alkoxy, S-alkyl, SO₂-alkyl, O-alkenyl, S-alkenyl, NR₁₅C(O)R₁₅, NR₁₅SO₂R₁₅, $N(R_{15})_{2}$ (D)-cycloalkyl, (D)-aryl (wherein aryl is phenyl or naphthyl), (D)-heteroaryl, (D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted, and two adjacent R₃ may form a 4- to 7-membered ring; each R4 is independently: hydrogen, alkyl, C(O)-alkyl, SO₂alkyl, SO₂aryl, (D)-aryl or

(D)-cycloalkyl;

each R₅ is independently:

hydrogen,

alkyl,

- (D)-aryl,
- (D)-heteroaryl,
- (D)-N(R_7)₂,
- (D)-NR7C(O)-alkyl,
- (D)-NR7SO2-alkyl,
- (D)-SO₂N(R₇)₂,
- (D)-(O)_q-alkyl,
- (D)-(O) $_q$ (D)-NR $_7$ COR $_7$,
- $(D)-(O)_{q}(D)-NR_{7}SO_{2}R_{7}$
- (D)-(O)q-heterocyclyl or
- (D)-(O)_q(alkyl)-heterocyclyl;

each R₆ is independently:

hydrogen,

alkyl,

- (D)-phenyl,
- C(O)-alkyi,
- C(O)-phenyl,
- SO₂-alkyl or
- SO₂-phenyl;

R₇ and R₈ are each independently:

hydrogen,

alkyl or

(D)-cycloalkyl, or

 R_7 and R_8 together with the nitrogen to which they are attached form a 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S and NR₄,

wherein alkyl and cycloalkyl are unsubstituted or substituted;

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R<sub>10</sub> is independently:
           hydrogen,
           alkyl,
           (D)-aryl or
           (D)-cycloalkyl;
 R<sub>11</sub> is:
          hydrogen or
          alkyl;
R<sub>12</sub> is:
          hydrogen,
          halo,
          alkyl,
          alkoxy,
          C≡N,
          CF<sub>3</sub> or
         OCF<sub>3</sub>;
R<sub>13</sub> is independently:
         hydrogen,
         hydroxy,
         cyano,
         nitro,
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halo,

alkyl,

alkoxy,

haloalkyl,

- (D)-C(O)R₁₅,
- (D)-C(O)OR₁₅,
- (D)-C(O)SR₁₅,
- (D)-C(O)-heteroaryl,
- (D)-C(O)-heterocyclyl,
- (D)-C(O)N(R_{15})₂,
- (D)-N(R₁₅)₂,
- (D)-NR₁₅COR₁₅,
- (D)-NR₁₅CON(R₁₅)₂,
- (D)-NR₁₅C(O)OR₁₅,
- (D)-NR₁₅C(R₁₅)=N(R₁₅),
- (D)-NR₁₅C(=NR₁₅)N(R₁₅)₂,
- (D)-NR₁₅SO₂R₁₅,
- (D)-NR₁₅SO₂N(R₁₅)₂,
- (D)-NR₁₅(D)-heterocyclyl,
- (D)-NR₁₅(D)-heteroaryl,
- (D)-OR₁₅,
- OSO₂R₁₅,
- (D)-[O]_q(cycloalkyl),
- $(D)-[O]_q(D)$ -aryl,
- (D)-[O]_q(D)-heteroaryl,
- (D)- $[O]_q(D)$ -heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen when q=1),
- (D)-SR₁₅,
- (D)-SOR₁₅,
- (D)-SO₂R₁₅ or
- (D)-SO₂N(R₁₅)₂,

wherein alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl and heteroaryl are unsubstituted or substituted;

each R₁₅ is independently:

hydrogen,

alkyl,

haloalkyl,

- (D)-cycloalkyl,
- (D)-aryl (wherein aryl is phenyl or naphthyl),
- (D)-heteroaryl,
- (D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and

wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted;

R₁₇ is independently:

R₁₀ or

(D)-heterocyclyl;

R₁₈ is independently:

R₁₀,

- (D)-heteroaryl,
- (D)-heterocyclyl,
- (D)- $N(Y)_{2}$,
- (D)-NH-heteroaryl or
- (D)-NH-heterocyclyl,

wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted, or

two R_{18} groups together with the atoms to which they are attached form a 5-to 8-membered mono- or bi-cyclic ring system optionally containing an additional heteroatom selected from O, S, NR_{10} , NBoc and NZ;

Cy is: aryl, 5- or 6-membered heteroaryl, 5- or 6-membered heterocyclyl or 5- or 7-membered carbocyclyl; Cy' is: benzene, pyridine or cyclohexane; X is: alkyl, (D)-cycloalkyl, (D)-aryl, (D)-heteroaryl, (D)-heterocyclyl, (D)-C≡N, (D)-CON(R₁₇R₁₇), (D)-CO₂R₁₇, (D)-COR₁₇, (D)-NR₁₇C(O)R₁₇, (D)-NR₁₇CO₂R₁₇, (D)-NR₁₇C(O)N(R₁₇)₂, (D)-NR₁₇SO₂R₁₇,

(D)-S(O)_pR₁₇,

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(D)-SO<sub>2</sub>N(R_{17})(R_{17}),
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- (D)-OR₁₇,
- (D)-OC(O)R₁₇,
- (D)-OC(O)OR₁₇,
- (D)-OC(O)N(R_{17})₂,
- (D)-N(R₁₇)(R₁₇) or
- (D)- $NR_{17}SO_2N(R_{17})(R_{17})$,

wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted;

Y is:

hydrogen,

alkyl,

- (D)-cycloalkyl,
- (D)-aryl,
- (D)-heterocyclyl or
- (D)-heteroaryl,

wherein aryl, heteroaryl, alkyl, D and cycloalkyl are unsubstituted or substituted;

Q is a bond, O, S(O)u, NR6 or CH2;

D is a bond or C₁ - C₄ alkyl;

E is O, S or NR₆;

G is D, CH-alkyl, O, C=O or SO_2 , with the proviso that when G is O, the ring atom M is carbon;

J is N or CH;

M is $CHCO_2Y$, $CHC(O)N(Y)_2$, NSO_2R_{18} , $CHN(Y)COR_{18}$, $CHN(Y)SO_2R_{18}$, $CHCH_2OY$ or $CHCH_2$ heteroaryl;

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T is O or NR<sub>7</sub>;

n is 0 - 3;

m is 1 - 3;

o is 0 - 3;

p is 0 - 2;

q is 0 or 1;

r is 1 or 2;

s is 0 - 3;

u is 0 - 2.
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2. The compound of claim 1, wherein

 R_1 is (D)-aryl which may be substituted with one to three substituents independently selected from the group consisting of cyano, nitro, perfluoroalkoxy, halo, alkyl (D)-cycloalkyl, alkoxy, hydroxy and haloalkyl;

$$(R_{5})_{s} (R_{3})_{s}$$

$$(R_{5})_{s} (R_{5})_{s}$$

R₃ is independently:

hydrogen,

halo,

alkyl,

hydroxy,

alkoxy,

S-alkyl,

SO₂-alkyl,

O-alkenyl,

S-alkenyl,

haloaikyl or

(D)-cycloalkyl;

R₄ is:

hydrogen or

alkyl;

each R₅ is independently:

hydrogen,

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alkyl,
          (D)-aryl,
          (D)-heteroaryl,
          (D)-N(R<sub>7</sub>)<sub>2</sub>,
          (D)-NR7C(O)alkyl or
          (D)-NR7SO2alkyl;
 R_7 and R_8 are each independently:
         hydrogen,
         alkyl or
         cycloalkyl, or
         R<sub>7</sub> and R<sub>8</sub> together with the nitrogen to which they are attached form a 5- to
         7-membered ring optionally containing an additional heteroatom selected from
         O, S and NR<sub>4</sub>;
R<sub>9</sub> is:
         alkyl,
         OR10,
        (D)-aryl,
        (D)-cycloalkyl,
        (D)-heteroaryl and
        halo;
R<sub>12</sub> is:
        hydrogen,
        halo,
        alkyl,
        alkoxy or
       C≡N;
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R<sub>13</sub> is independently:
                 hydrogen,
                 hydroxy,
                 cyano,
                 nitro,
                halo,
                alkyl,
                alkoxy,
                haloalkyl,
               (D)-C(O)-heterocyclyl,
               (D)-N(R<sub>15</sub>)<sub>2</sub>,
               (D)-NR<sub>15</sub>COR<sub>15</sub>,
               (D)-NR<sub>15</sub>CON(R<sub>15</sub>)<sub>2</sub>,
               (D)-NR<sub>15</sub>C(O)OR<sub>15</sub>,
              (D)-NR<sub>15</sub>C(R<sub>15</sub>)=N(R<sub>15</sub>),
              (D)-NR<sub>15</sub>C(=NR<sub>15</sub>)N(R<sub>15</sub>)<sub>2</sub>,
              (D)-NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub> or
              (D)-NR<sub>15</sub>SO<sub>2</sub>N(R<sub>15</sub>)<sub>2</sub>;
 each R<sub>14</sub> is independently:
             hydrogen,
             halo,
             alkyi,
            (D)-cycloalkyl,
             alkoxy or
            phenyl;
each R<sub>15</sub> is independently:
           hydrogen,
            halo,
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alkyl,
         (D)-cycloalkyl,
         alkoxy or
         phenyl;
 each R<sub>16</sub> is independently:
         hydrogen,
         alkyl or
         cycloalkyl;
X is:
         alkyl,
         (D)-cycloalkyl,
         (D)-aryl,
         (D)-heteroaryl,
        (D)-heterocyclyl,
        (D)-NHC(O)R_{17},
        (D)-CO<sub>2</sub>R<sub>17</sub> or
        (D)-CON(R_{17}R_{17});
Y is:
        hydrogen,
        alkyl,
        (D)-cycloalkyl,
        (D)-aryl,
        (D)-heterocyclyl or
        (D)-heteroaryi;
Cy is:
        aryl,
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5- or 6-membered heteroaryl,5- or 6-membered heterocyclyl or5- to 7-membered carbocyclyl;
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Cy' is benzene or pyridine; 
D is a bond or C_1 - C_4-alkylene; 
M is NSO_2R_{18}, CHN(Y)COR_{18} or CHN(Y)SO_2R_{18}; 
G is D or CH-alkyl; 
T is NR_7 or O; 
n is 0 or 1; 
m is 1 or 2; 
r is 1; 
s is 0, 1 or 2.
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3. The compound of claims 1 or 2, wherein

 R_1 is (D)-phenyl or (D)-naphthyl which may be substituted with one or two substituents independently selected from the group consisting of perfluoroalkoxy, halo, alkyl, alkoxy and haloalkyl;

R₃ is hydrogen or halo;

R₄ is hydrogen;

R₅ is hydrogen;

 R_7 and R_8 are each independently:

hydrogen or

alkyl, or

 R_7 and R_8 together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

R₁₂ is:

hydrogen,

halo or

C₁ - C₄ alkyl;

R₁₃ is independently:

cyano,

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nitro,
            halo,
            alkyl,
           (D)-C(O)-heterocyclyl,
           (D)-N(R_{15})_2,
           (D)-NR<sub>15</sub>COR<sub>15</sub>,
           (D)-NR<sub>15</sub>CON(R<sub>15</sub>)<sub>2</sub>,
           (D)-NR<sub>15</sub>C(O)OR<sub>15</sub> or
           (D)-NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub>;
 each R<sub>14</sub> is independently:
           hydrogen,
           halo,
           alkyl,
          alkoxy or
          phenyl;
each R<sub>15</sub> is independently:
          hydrogen,
          halo,
          alkyl,
          alkoxy or
          phenyl;
X is:
         alkyl,
         (D)-cycloalkyl,
         (D)-heterocyclyl,
         (D)-NHC(O)R<sub>17</sub> or
         (D)-CON(R_{17}R_{17});
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Y is:

hydrogen,
alkyl,
(D)-cycloalkyl or
(D)-heterocyclyl;

Cy is

aryl or
5- or 6-membered heteroaryl;

Cy' is benzene;
D is a bond or CH<sub>2</sub>;
M is NSO<sub>2</sub>R<sub>18</sub>;
G is D;
s is 0 or 1.
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4. The compound of any of claims 1 to 3, wherein

 R_1 is (CH_2) -phenyl or (CH_2) -naphthyl which may be substituted with one to three halo atoms;

$$(R_5)_s \qquad (R_3)_s \qquad (R_3$$

R₁₂ is hydrogen;

R₁₃ is independently:

cyano,

nitro,

halo or

(D)-NR₁₅COR₁₅;

X is:

C₁ - C₄ alkyl,

C₅ - C₇ cycloalkyl,

(D)-CON($R_{17}R_{17}$) or

N-containing heterocyclyl;

Y is:

hydrogen,

C₁ - C₄ alkyl or

C₅ - C₇ cycloalkyl;

Cy is aryl;

G is CH₂.

- 5. The compound of any of claims 1 to 4 for use as a medicament.
- 6. Use of the compound of any of claims 1 to 4 for the preparation of a medicament for the treatment or prevention of disorders, diseases or conditions responsive to the modulation of the melanocortin-4 receptor in a mammal, where modulation means activation in the case of MC4-R agonists or inactivation in the case of MC4-R antagonists.
- Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of cancer cachexia.
- Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of muscle wasting.
- Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anorexia.
- 10. Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anxiety and/or depression.
- Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of obesity.
- Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of diabetes mellitus.

AMENDED SHEET (ARTICLE 19)

- 13. Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of male or female sexual dysfunction.
- 14. Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of erectile dysfunction.
- 15. A pharmaceutical composition which comprises a compound of any of claims 1 to 4 and a pharmaceutically acceptable carrier.